

**IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	Master File No. 2:12-MD-02327 MDL 2327
THIS DOCUMENT RELATES TO: WAVE 3 CASES	JOSEPH R. GOODWIN U.S. DISTRICT JUDGE

**DEFENDANTS' REPLY IN SUPPORT OF MOTION TO EXCLUDE
THE OPINIONS AND TESTIMONY OF VLADIMIR IAKOVLEV, M.D.**

Defendants Ethicon, Inc. and Johnson & Johnson (collectively, “Ethicon”) submit this Reply in Support of their Motion to Exclude the Testimony and Opinions of Vladimir Iakovlev, M.D. [Doc. 2850]. In Wave 3, Ethicon adopted and incorporated by reference its Wave 1 Motion to Exclude the Opinions and Testimony of Vladimir Iakovlev, M.D. [Doc. 2066 (“Mot.”)] and Memorandum of Law in Support [Doc. 2070 (“Mem.”)], (collectively, “Motion”).

To the extent that Plaintiffs’ Response to the Motion [Doc. 2959 (“Response”)] incorporates by reference their Wave 1 *Daubert* Response [Doc. 2185], Ethicon incorporates by reference its Reply in Support of its Motion to Exclude the Testimony and Opinions of Vladimir Iakovlev, M.D. [Doc. 2251].

Because Plaintiffs also asserted certain additional responses, Ethicon submits the following reply addressing Plaintiffs’ new arguments.

I. Dr. Iakovlev's Failure To Follow The Methodology Used By Pathologists To Orient Specimens *In Vivo* Renders His Opinions Regarding Mesh Folding And Deformation Speculative And Unreliable.

In its Motion, Ethicon explained that Dr. Iakovlev's opinions regarding mesh folding, curling, and deformation are unreliable because he failed to follow the standard methodology used by pathologists to determine how the mesh was oriented *in vivo*. Mem. at 20-21. In Wave 1, this Court excluded Dr. Iakovlev's mesh folding and deformation opinions "to the extent they rely solely on his personal analysis of pathology slides[.]" Mem. Op. and Order (*Daubert* Motion re: Vladimir Iakovlev, M.D.), at 8 [Doc. 2710] ("Wave 1 *Daubert* Order").

Although Plaintiffs ask the Court to reconsider this ruling, none of their arguments actually address the critical flaw in Dr. Iakovlev's mesh folding and deformation opinions—his failure to follow the standard methodology used by pathologists to determine mesh orientation and placement in the human body. Nothing in Plaintiffs' response supports the proposition that a pathologist can look at a pathology slide and determine that mesh folded or deformed in the human body prior to explantation.

A. Dr. Iakovlev's opinions regarding mesh folding and deformation are not the product of a reliable methodology.

As an initial matter, Plaintiffs simply disregard the fact that Dr. Iakovlev has admitted that he cannot determine whether mesh folds or deforms during the implantation surgery or post-implantation. Mem. at 21 (citing Dr. Iakovlev's testimony). The Court should reject Plaintiffs' arguments on this basis alone.

Similarly, Plaintiffs' Response does not even address the fact that the methodology described in Ethicon's Motion—which is the standard methodology set forth in pathology textbooks—is the proper method for determining the orientation and condition of the specimen as it existed in the human body. *See* Resp. at 3-6 (discussing the standard methodology explained

in Mot. Ex GG, William Westra, *et al.* Surgical Pathology Dissection 4 (2003) and Mot. Ex. HH, Susan Lester, Manual of Surgical Pathology 7, (2010)). Nor do Plaintiffs claim that Dr. Iakovlev used this methodology in his analysis.

Instead, Plaintiffs argue that Dr. Iakovlev's mesh folding and deformation opinions are reliable because he has grossly and microscopically examined explants "following the same methodology as is done by him and other pathologists around the world every day[.]" Resp. at 4. Plaintiffs' argument is not only incorrect, but it simply misses the point.

As explained in standard pathology textbooks like Westra and Lester, a pathologist's failure to follow the appropriate methodology for determining the condition of a specimen as it existed *in vivo* renders any conclusion as to its appearance speculative. *See* Mot. at 21 (citing Mot. Ex. GG, Westra at 4 and Mot. Ex. HH, Lester at 7). No part of Plaintiffs' recitation of the generic pathology methods purportedly followed by Dr. Iakovlev speaks the orientation of specimens *in vivo*. *See* Resp. at 4; *see also id.* at 6. In fact, nothing in Plaintiffs' Response or Dr. Iakovlev's expert reports or testimony supports the proposition that a pathologist can determine whether a mesh folded or deformed *in vivo*, merely by looking at a slide without following the appropriate methodology described in pathology textbooks.

Even assuming the generic methodology Plaintiffs describe in their Response is reliable in the context of general pathology opinions, that methodology does not define how a pathologist determines the orientation of specimens as they existed *in vivo*. For this reason, Dr. Iakovlev's use of that generic methodology does not permit him to offer reliable opinions about how mesh appeared in the human body. *See Huskey v. Ethicon, Inc.*, 29 F. Supp. 3d 691, 702 (S.D. W. Va. 2014) ("scientific validity for one purpose is not necessarily scientific validity for other unrelated

purposes”) (quoting *Daubert*, 509 U.S. at 591-92). Plaintiffs’ entire argument is nothing but a bait-and-switch.

Plaintiffs do not deny that Dr. Iakovlev failed to follow the standard methodology used by pathologists to determine the *in vivo* appearance of specimens. Thus, Plaintiffs’ assertion that Dr. Iakovlev’s mesh folding and deformation opinions “are based on sound methodology employed by other pathologists in the field” is simply false.

B. The articles or reports to which Plaintiffs cite do not permit Dr. Iakovlev to offer opinions about mesh folding or deformation without following the appropriate methodology.

Plaintiffs also claim that Dr. Iakovlev’s mesh folding and deformation opinions are reliable because they are based on certain articles and operative reports. Resp. at 4-5. Plaintiffs misunderstand both Ethicon’s argument and the Court’s order.

Ethicon’s position is not that mesh *cannot* fold or deform; rather, Ethicon argues that Dr. Iakovlev’s failure to adhere to the appropriate methodology renders speculative and unreliable any opinion that a mesh folded or deformed *in vivo* based on his review of a pathology slide. Mem. at 20-22. Ethicon’s position is consistent with this Court’s Order that Dr. Iakovlev cannot offer opinions regarding mesh folding and deformation based on his personal analysis of pathology slides. This is a different issue than a urogynecologist testifying that a mesh was folded or bunched based on a description in an explant operative report. Nothing in any of the articles or reports to which Plaintiffs cite supports Dr. Iakovlev’s position that he can detect this folding based on the appearance of processed tissue in a two-dimensional slide.¹

¹ To the extent Plaintiffs suggest that Dr. Iakovlev should be able to opine about mesh folding or deformation because *all* meshes fold or deform *in vivo*, none of the literature to which they cite supports that flawed assertion.

Ultimately, Plaintiffs failed to identify any scientific literature that affects this Court's Wave 1 ruling, and the Court should preclude Dr. Iakovlev from opining about mesh folding or deformation at trial based on his evaluation of pathology slides.

II. Dr. Iakovlev's Opinions Regarding Complications Allegedly Caused By Ethicon Mesh Products Is Unreliable And Speculative.

In its Motion, Ethicon explained that Dr. Iakovlev's opinions that Ethicon mesh products cause complications in women are unreliable because they are based on his histological observations rendered in the absence of an asymptomatic control. *See* Mem. at 11-12. This Court excluded Dr. Iakovlev's "complications opinions based on his examination of explanted mesh samples without the use of a control sample," on the grounds that such opinions were not the product of "a sufficiently reliable methodology." Wave 1 *Daubert* Order, at 8-9.

Plaintiffs argue that the Court's ruling was erroneous because the use of a control is "neither required nor practiced in the field of pathology." Resp. at 10. Specifically, Plaintiffs assert that a pathologist does not use controls because they rely solely on their "knowledge of normal histology." *Id.* at 8; *see also id.* at 10. Plaintiffs' argument is unsupported by medical literature, and inconsistent with basic principles of science.

A. Dr. Iakovlev's failure to use a control is inconsistent with basic scientific principles, and Plaintiffs assertions to the contrary are unfounded in science.

Ethicon explained in its Motion that Dr. Iakovlev's opinions regarding the complications allegedly caused by Ethicon mesh products is unreliable because he refused to compare his histological findings to a control specimen. *See* Mem. at 11. Ethicon showed that, without a control, Dr. Iakovlev cannot reliably draw any causal conclusions because he cannot say that his histological findings regarding a patient suffering from a particular complication are different than the histological presentation of patients not suffering from that complication. *See id.*

Ethicon’s argument that Dr. Iakovlev’s opinions are unreliable in the absence of a control is based on fundamental principles of science. Plaintiffs have pointed to no authority suggesting that pathology is somehow exempt from such core scientific principles. *Cf.* Reply Ex. JJ, Robbins & Cotran Pathologic Basis of Disease, at 11 (8th Edition 2010) (explaining that pathology “serves as the bridge between the basic sciences and clinical medicine, and is the scientific foundation for all medicine.”).

The importance of using a control in the context of pathology is demonstrated in studies like Hill’s *Histopathology of Excised Midurethral Sling Mesh*, 26 Int’l Urogynecology J. 591 (2015) (attached to Ethicon’s Motion as Exhibit C). In that study, the authors hypothesized that inflammation was positively correlated with pain. *Id.* at 592. But unlike Dr. Iakovlev, the Hill study authors compared the histopathology findings regarding explants from patients complaining of pain with those of patients who did not. *Id.* Contrary to their own hypothesis, the authors found that pain was not associated with increased inflammation. *Id.* at 592-93. Thus, the Hill study reinforces the scientific significance of using a control.

In response to Ethicon’s arguments, Plaintiffs simply assert that Dr. Iakovlev did not need to use a control because a pathologist’s “knowledge of normal histology” functions as a control. Resp. at 8.² Plaintiffs’ argument is unsupported by scientific or medical literature, and is ultimately nonsensical.

First, Dr. Iakovlev lacks statistically valid sample of normal tissue from asymptomatic meshes to serve as the “de facto control.” The explanted meshes that Dr. Iakovlev sees are for litigation purposes and, by definition, involve women who claim that they are symptomatic. Dr.

² Plaintiffs set up a straw man in claiming that the Court’s ruling “begs the question” as to “[w]hat constitutes a ‘proper control’ in the context of a pathologist employing well-accepted, standard methodology in arriving at a pathological diagnosis[.]” Resp. at 7. Plaintiffs fail to grasp the fact that Dr. Iakovlev’s failure to use a control in the first place demonstrates that he did not, in fact, “employ[] a well-accepted, standard methodology.”

Iakovlev has conceded that he has not inspected enough asymptomatic meshes to have a statistically valid sample. *See* Reply Ex. KK, Iakovlev 3/5/2016 *Massey* Dep. at 49:22-50:12 (“To this date I was checking if I have asymptomatic or painless—or patients who did not complain or did not report pain which was entered in the record. The number was so small that statistically would be difficult to compare. I mean [the power of that study] would be probably invalid[.]”). In other words, whether his comparison of the tissue is formal or informal, he has no control to use as a comparator.

Second, the notion that an individual’s memory of how a specimen normally looks constitutes a valid control would eliminate the need for a control in any circumstance in which the individual analyzing a specimen had previously seen a “normal” specimen. Plaintiffs’ suggestion is unsupported and has no basis in science.

Ultimately, Plaintiffs cannot evade bedrock scientific principles by declaring controls unnecessary simply because Dr. Iakovlev states that he does not need one. *See* Resp. at 9-10 (asserting that pathologists are not required to use controls based on Dr. Iakovlev’s affidavit). Plaintiffs’ arguments are contrary to the scientific method, and should be rejected by this Court.

B. Plaintiffs’ suggestion that a control is unnecessary in the field of pathology has no basis in science or medicine.

Although the crux of Plaintiffs’ argument is that pathologists do not use controls in their practice, they fail to cite a single piece of scientific or medical literature supporting their assertion. *See* Resp. at 7-10. In fact, Plaintiffs base their argument solely on an affidavit by Dr. Iakovlev and his expert report. *See id.* But, tellingly, neither Dr. Iakovlev’s affidavit nor his expert report identify any literature supporting the notion that controls are unnecessary in the field of medicine or the subspecialty of pathology. *See generally* Resp. Ex. I, Affidavit of

Vladimir Iakovlev, MD, FRCPC, FCAP (“Iakovlev Aff.”); Mot. Ex. D, Expert Report of Vladimir Iakovlev.

Thus, Plaintiffs’ argument rests solely on Dr. Iakovlev’s *ipse dixit*, which does not constitute a reliable basis for his opinions. *See Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) (“nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert.”). For this reason alone, the Court should preclude Dr. Iakovlev from offering opinions about complications based on his analysis of pathology slides.

Plaintiffs’ efforts to obscure the dearth of support for their position by citing Robbins and Cotran are nothing but a bait-and-switch. *See* Resp. at 7-8. Nothing in Plaintiffs’ Response, Dr. Iakovlev’s affidavit, or Robbins and Cotran itself shows that it stands for the proposition that pathologists do not use controls in their histological analyses. Indeed, both Plaintiffs and Dr. Iakovlev point to Robbins and Cotran only for generic descriptions of pathology. *See* Resp. at 7-8; Resp. Ex. I, Iakovlev Aff. at ¶¶ 1-3.

Moreover, although Dr. Iakovlev now claims in his affidavit that Robbins and Cotran serves as the basis for his methodology, his expert report shows that his sole reference to that text is for the proposition that “[i]n adult mammals, regeneration of soft tissue may occur to a limited degree in some animals.” Mot. Ex. D, Iakovlev Report at 6, 127. In other words, Plaintiffs’ assertion that Robbins and Cotran constitutes the foundational predicate of Dr. Iakovlev’s methodology is disingenuous, at best.

Ultimately, Plaintiffs were unable to identify any scientific or medical support that provides a methodological basis for Dr. Iakovlev’s failure to incorporate an asymptomatic control in his analysis. For this reason, the Court should preclude Dr. Iakovlev from offering

complications opinions based on his review of pathology slides in the absence of a control specimen.

C. Plaintiffs misstate the law under *Daubert*.

Finally, Plaintiffs claim that Dr. Iakovlev should be permitted to opine about the complications without incorporating a control in his analysis because he does not use a control in his normal practice. Resp. at 9-10. In attempting to support their argument, Plaintiffs assert that “[f]ederal [c]ourts in this country agree that an expert’s opinion is admissible under *Daubert* where the expert employs the same methodology in litigation that *the expert* applies in practice.” Resp. at 10 (emphasis added). Plaintiffs misunderstand *Daubert* and its progeny.

As the decisions Plaintiffs cite demonstrate, the case law clearly states that the proper metric is the “practice of *an* expert in the relevant field,” not the practice of the expert himself. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999); *Cooper v. Smith & Nephew, Inc.* 259 F.3d 194, 200 (4th Cir. 2001); *Eghnayem v. Boston Sci. Corp.*, 57 F. Supp. 3d 658, 675 (S.D. W. Va. 2014). Under Plaintiffs’ nonsensical reading, an expert’s opinion would be reliable—even if he failed to comply with the scientific method—so long as he used the same baseless methodology in his practice. Nothing in *Daubert* or its progeny supports such an absurd result.

Plaintiffs cannot transform Dr. Iakovlev into the arbiter of the reliability of his own opinions, and the Court should reject Plaintiffs’ arguments on this basis.

III. Conclusion

For these reasons, as well as those articulated in Ethicon’s Motion, Ethicon respectfully requests that the Court grant its Motion to Exclude the Opinions and Testimony of Dr. Vladimir Iakovlev.

Respectfully submitted,

/s/ David B. Thomas

David B. Thomas (W.Va. Bar #3731)
Philip J. Combs (W.Va. Bar #6056)
Thomas Combs & Spann PLLC
300 Summers Street
Suite 1380 (25301)
P.O. Box 3824
Charleston, WV 25338
(304) 414-1800
dthomas@tcspllc.com

/s/ Christy D. Jones

Christy D. Jones
Butler Snow LLP
1020 Highland Colony Parkway
Suite 1400 (39157)
P.O. Box 6010
Ridgeland, MS 39158-6010
601.985.4523
christy.jones@butlersnow.com

COUNSEL FOR DEFENDANTS ETHICON, INC.
AND JOHNSON & JOHNSON

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CERTIFICATE OF SERVICE

I hereby certify that on October 21, 2016, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to CM/ECF participants registered to receive service in this MDL.

/s/ David B. Thomas

David B. Thomas (W.Va. Bar #3731)
Philip J. Combs (W.Va. Bar #6056)
Thomas Combs & Spann, PLLC
300 Summers Street, Suite 1380
P.O. Box 3824
Charleston, WV 25338-3824
(304) 414-1800

COUNSEL FOR DEFENDANTS ETHICON, INC.
AND JOHNSON & JOHNSON